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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): AC-50-US

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on _____

Signature _____

Typed or printed name _____

Application Number	Filed
10/560,383	March 29, 2007

First Named Inventor: Michael G. Orchard et al.

Art Unit	Examiner
1625	John Mabry

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal. ✓

The review is requested for the reason(s) stated on the attached sheet(s). ✓
Note: No more than five (5) pages may be provided.

I am the:

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 58,337
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

Brittany La
Typed or printed name

973-912-5232
Telephone number

March 7, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Michael G. Orchard et al.	Examiner: John Mabry
Serial No.:	10/560,383	Group Art Unit: 1625
Filed:	March 29, 2007	Docket No.: AC-50-US
Title:	2-HYDROXYMETHYL-3,4,5-TRIHYDROXY-1-(4-PENTYLOXYBENZYL) PIPERIDINE AS GLYCOSYLCERAMIDE SYNTHASE (GCS) INHIBITORS	Confirmation No.: 9092

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

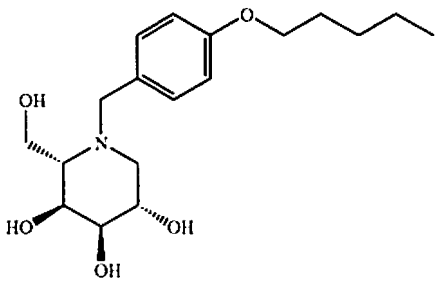
In response to the Final Office Action dated December 7, 2010 and the Advisory Action dated February 3, 2011, Applicants respectfully request for a Pre-Appeal Brief Review of this case for reversal of the Examiner's rejections of the claims based on clear errors. In support of the request, Applicants hereby submit the following and respectfully request for consideration:

Notice of Appeal — attached hereto;
PTO/SB/33 — attached hereto;
REMARKS — pages 2-5;
Exhibit A — Listing of the Claims – attached hereto;
Exhibit B – U.S. Appl. No. 10/522,207 – attached hereto

REMARKS

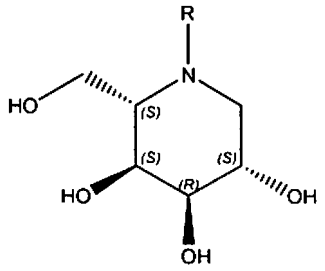
Claims 1, 3 and 20 are pending. Claims 2 and 5-19 were cancelled. Claims 4 and 21-35 were withdrawn. Claims 1 and 3 (and 20)[1] have been provisionally rejected for being unpatentable over claims 1-10 and 13 of co-pending application number 10/522,207 (the '207 application) on the ground of non-statutory obviousness-type double patenting.

Claim 1 of the current application is directed to the compound 3,4,5-piperidinetriol, 2-(hydroxymethyl)-1-[(4-(pentyloxy)phenyl)methyl]-, (2S,3S,4R,5S):



in free or a pharmaceutically acceptable salt form and claim 3 is directed to a composition comprising the same.

Claim 1 of the '207 application is directed to a compound of formula (I) in free or pharmaceutically acceptable salt form:



(I)

"wherein

R is -C_{1-3} alkylAr^1 where Ar^1 is phenyl;

wherein phenyl is substituted by one or more substituents selected from CN, $CON(R^1)_2$, SO_nR^2, $SO_2N(R^1)_2$, $N(R^5)_2$, $N(R^1)COR^2$, $N(R^1)SO_nR^2$, C_{0-6} alkylAr^2, C_{2-6} alkenylAr^2 and C_{3-6} alkynylAr^2...

[1] The Examiner noted in the Final Office Action Summary dated 12/7/2011 that claim 20 is allowable. The Advisory Action dated February 10, 2011 noted however, that claim 20 is rejected. Applicants hereby seek clarification as to the status of this claim.

and the Ar^1 phenyl is optionally substituted by one or more additional substituents selected from F, Cl, Br, CF_3, OCF_3, OR^3 and C_{1-6} alkyl: . . .

R^3 is H, or C_{1-6} alkyl;".

The Examiner argued that claims 1 and 3 of the current application are unpatentable in view of claims 1-10 and 13 of the '207 application because "the species of the instant application is encompassed by the genus as claimed in US '207". *Office Action* 12/7/2010, page 5. The Examiner therefore rejected the claims on the ground of obviousness-double patenting.

Applicants respectfully disagree. Applicants first take this opportunity to clarify the following: while it is true that the R substituent of the compound of Formula I of the '207 Application may be $-C_{1-3}$alkyl Ar^1 wherein the Ar^1 phenyl may optionally be substituted with one or more additional substituents selected from, among others, OR^3 wherein R^3 may be H or C_{1-6}alkyl, Applicants correct the statement made in the response filed February 7, 2011 and disagrees with the Examiner that the claims of the current application and the claims of the '207 application have patentably indistinct genus-species relationship. Generic claim 1 of the '207 application requires that the Ar^1 phenyl of the $-C_{1-3}$ alkylAr^1 be substituted with one or more substituents selected from "CN, $CON(R^1)_2$, SO_nR^2, $SO_2N(R^1)_2$, $N(R^5)_2$, $N(R^1)COR^2$, $N(R^1)SO_nR^2$, C_{0-6} alkylAr^2, C_{2-6} alkenylAr^2 and C_{3-6} alkynylAr^2..." and provides that Ar^1 phenyl may optionally be substituted with one or more additional substituents selected from, among others, OR^3 wherein R^3 may be H or C_{1-6}alkyl. (Emphasis added). As such, the Ar^1 phenyl is only additionally substituted with, among others, OR^3 if Ar^1 is first substituted with one or more substituents selected from "CN, $CON(R^1)_2$, SO_nR^2, $SO_2N(R^1)_2$, $N(R^5)_2$, $N(R^1)COR^2$, $N(R^1)SO_nR^2$, C_{0-6} alkylAr^2, C_{2-6} alkenylAr^2 and C_{3-6} alkynylAr^2...". In other words, OR^3 substituent is a selection when Ar^1 phenyl is di-, tri-substituted, etc. In contrast, the compound of the currently claimed invention is specifically mono-substituted at the benzyl substituent with a pentyloxy group. Consequently, the compound of the current invention is patentably distinct from those claimed in the '207 application and the Examiner has erroneously interpreted the claims in the '207 application.

Even if the claims of the current invention have a genus-species relationship with the claims of the '207 application, MPEP 804 explicitly warned that: "[d]omination [i.e., when one patent or application has a broad or generic claim which fully encompasses or reads on an

invention defined in a narrower or more specific claim in another patent or application] by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection." MPEP 804, citing *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964). If not based on anticipation, the obviousness-type double patenting determination should parallel the guidelines for a 35 U.S.C. 103(a) rejection. MPEP 804. In this regard, the Federal Circuit has held that a disclosure of a generic formula does not by itself render obvious a species of that genus, *See In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.")(Citation omitted). Extending the analysis of *Baird*, a claim covering a genus does not by itself render a claim covering the species patentably indistinct and unpatentable.

In analyzing obviousness under § 103(a), the Federal Circuit clearly stated in *Eisai Co. LTD v. Dr. Reddy's Laboratories, LTD.*, 533 F.3d 1353 (Fed. Cir. 2008) that "a prima facie case of obviousness for a chemical compound [ ] begins with the reasoned identification of a lead compound." *Id.* at 1359. Also in *Takeda Chemical Industries, LTD v. Alpharm PTY., LTD*, 492 F.3d 1350 (Fed. Cir. 2007), the Court stated that "[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure." *Id.* at 1356. In the recent case *Daiichi Sankyo Co., LTD. v. Matrix Lab. LTD.*, 2010 WL 3504759 (Fed. Cir. 2010), the Court again reiterated that "proving a reason to select a compound as a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds. [] Potent and promising activity in the prior art trumps mere structural relationships." *Id.* at *5 (emphasis added). In particular, the Court explained: "it is the possession of promising useful properties in a lead compound that motivates a chemist to make structurally similar compounds", warning that "attribution of a compound as a lead compound after the fact must avoid hindsight bias". *Id.*

Here, the Examiner committed clear errors in interpreting the claims of the '207 application to be patentably indistinct from the claims of the current invention. The Examiner further committed clear errors in ignoring the explicit warning in MPEP Section 804 and

rejecting the claims of the current invention based solely on the erroneous ground that claims of the co-pending '207 application dominates the claims of the current application. In doing the obviousness-type double patenting analysis, the Examiner also failed to provide any rationale whatsoever as to why the claims of the current invention are obvious and patentably indistinct from those of the '207 application. Specifically, the Examiner failed to follow the lead-compound test by failing to identify a reason for plucking the $-OR^3$ substituent from the group of substitutents listed in claim 1 of the '207 application and ignoring that the Ar^1 phenyl must also be substituted with other specific substituents so as to arrive at the current invention. None of the specific compounds claimed in claim 11 are actual exemplification of a compound wherein Ar^1 phenyl is additionally substituted with OR^3. Nothing in the claims (or the specification) of the '207 application points a skilled artisan to select the currently claimed compound as the compound of choice to pursue out of a large number of possibilities. The Examiner can only identify the currently claimed compound as the compound of choice based on improper hindsight knowledge of the current invention.

Wherein the Examiner has misinterpreted the claims in the '207 application, failed to express a well-reasoned analysis and used hindsight knowledge of the current invention to select from the possibilities set out in claims of the '207 application, the specific substituents so as to arrive at the current invention, the Examiner has committed clear errors in the obviousness-type double patenting analysis. Reconsideration and reversal of the rejections of claims 1 and 3 (and 20) are earnestly requested.

Respectfully submitted,

Dated: March 7, 2011

By _____

Brittany La
Reg. No. 58,337
HOXIE & ASSOCIATES L.L.C.
75 Main Street, Suite 301
Millburn, NJ 07041
(973) 912-5232